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South Asia Edition

Medicines play a vital role in eye care. INDIA

Medicines for eye health

Teamwork is vital if we want to support patients to access and use their eye medication.

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Medicines have a vital role in eye care, not only when patients are in the hospital or eye clinic, but also when they have to continue caring for their eyes at home.

For patients to adhere with the prescribed use of eye medicines, two conditions must be met:

1 The medication prescribed must be locally available, at a cost the patient can afford (also in the long term if they have a chronic eye condition). To address this, we have included articles on advocacy, local production of eye drops, and the management of eye medicines in a hospital or clinic setting.

2 Patients must also understand how and why to use their eye medication. We therefore have an article on empowering patients and a one-page instruction sheet which you can copy and share directly with patients.

Each member of the eye care team has a role in meeting these two conditions, and good communication is essential.

- **Pharmacists** can check prescriptions for safety and accuracy, give feedback to clinicians, and support patient education and adherence.
- **Clinicians and prescribers** can ask pharmacists which medicines are locally available and affordable.
- **Nurses and allied health personnel** can support patients by checking they have the correct prescription and/or medication before leaving the hospital, and by teaching them how to use their medication correctly.
- **Managers and policy makers** can support advocacy efforts or consider producing eye drops locally.

However, as we hope to show in this issue, these eye care team members will be most effective in their role if they can recognise that the patient is the most important member of the eye care team. If the patient's needs, abilities, circumstances and preferences are not taken into account at every step, adherence will remain a challenge and even the best medication will not be effective.

About this issue

Medicines play a vital role in eye care; not only in the hospital, but also when patients must care for their eyes at home. Ensuring the availability, safety and effective use of eye medicines requires a team effort, with patients and their needs firmly at the centre.

Contents

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Management of medicines in an eye hospital

Medication management is essential for safe and effective eye care.

Medication forms a large part of ophthalmic treatment – a significant proportion of patients who undergo outpatient consultation at tertiary eye care facilities and primary eye care facilities are prescribed medication.

So it is important that the management of eye medication is integrated into eye care services at all levels. Great advancements in ocular medication therapy have resulted in a wide range of medicines being available, each with a specific use. This complexity makes it crucial for hospitals to implement a systematic and safe approach to drug dispensing. Without proper protocols, errors in medication dispensing can have serious consequences for patients.[1]

The hospital or clinic pharmacy

A hospital or clinic pharmacy is required to manage stock of medication for two distinct purposes:

1 Medicines used within the clinic for diagnosis and procedures. These include dilating drops, anaesthetic drops, and medication used for emergency treatment or during surgery.

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INTERNATIONAL CENTRE FOR EYE HEALTH

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

IAPB

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2 Medicines prescribed and dispensed to the patient for use at home. Some hospitals will give the patient a prescription to take to a pharmacy in the community.

The medications stocked in a hospital-based pharmacy depends on the services provided. For example, primary and secondary care facilities will stock common ocular medication used for allergies and infections, and tertiary care facilities may stock a more complex variety of medications for conditions such as glaucoma, diseases of the uveal tract, etc.

It is important to have a holistic view of the medications that patients may need. For instance, although glaucoma is not treated at a primary eye care facility, it would be helpful to stock common glaucoma medicines so that patients are able to get refills locally.

Standardisation

It is important to standardise the list of medications and the brands that a hospital will use or dispense. This allows better price negotiation and stock management, and can help to ensure the quality and efficacy of the drugs.

Prescription writing

A legible and complete prescription is essential for safe drug dispensing.

Prescriptions should be written **legibly** – possibly in capital letters. Where possible, printed prescriptions are preferred.

Prescriptions must be **complete**. It must have the patient's name and medical record number, the name of the drug, the strength, dosage, and duration. Any special instructions should be clearly and unambiguously written. Prescriptions must also carry the doctor's name and signature, and the date.

Ensure that only authorised personnel are permitted to prescribe medication. If an assistant writes down a doctor's orders, a policy of reading back what was written will help to prevent errors.

Where possible, give patients a consolidated set of instructions that factors in drugs from previous prescriptions as well as those prescribed at the latest visit.

A pharmacy assistant counsels a patient about his eye medicines and how to use them. INDIA

Inventory management

Having an adequate supply of medicines in stock helps to ensure that patients receive treatment without delay. Medicines must be in date, and of good quality. It is therefore important to monitor stock levels (inventory) on a regular basis, and to check the quality of purchased medicines as they come in: check for any leakage, discoloured liquids, contamination, etc.

It is also important to develop good working relationships with a few reliable suppliers, as this can help hospitals to avoid fake drugs, negotiate better prices, and ensure sufficient stock levels. When there is a long-standing relationship, and mutual trust, suppliers may agree to replace medicines nearing their expiry date and respond to special drug requirements. Some suppliers may also provide stock on consignment, meaning that the hospital pays for medicines only when they have been sold.

Set up systems to ensure that stock is always dispensed according to a first-in, first-out method, so that medicines purchased first are dispensed first. Usually, this is done by stacking newly purchased packs at the back and dispensing packs from the front. A computerised inventory system can greatly enhance inventory management of drugs and alert staff about medicines nearing the expiry date.

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Look-alike medications are clearly labelled in this store room. INDIA

Storage and disposal

Always store medicines as recommended by the manufacturer. Make sure the storage area is well-lit, well-ventilated, and checked often to make sure no one is taking them without permission. Ensure that all medicines are kept at the correct temperatures.

Medicines that look alike and/or sound alike (also known as LASA) can result in dispensing and administering errors. Display a list of LASA drugs where pharmacists and other staff members can see it, and encourage the use of non-proprietary (generic) names for medicines. At Aravind, we train staff members to colour code LASA drugs and physically separate them within the storage area. Further guidance from the World Health Organisation is available at **bit.ly/WHOlasa**

Carry out regular audits to identify and remove expired drugs, and dispose of all medicines safely.

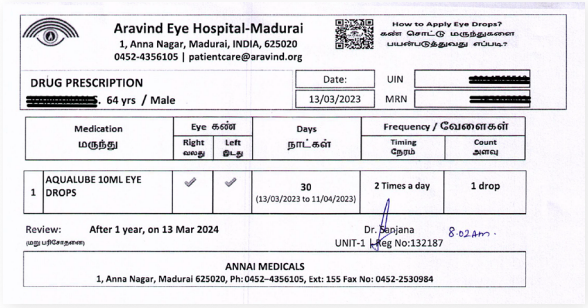
Safe dispensing

Processes at the pharmacy must be standardised to ensure that staff always verify the prescription, ensure correct drug, strength and quantity, correct billing, and handing over with clear instructions. Medicine dispensing must be accompanied with detailed do's and don'ts – including how to open the eye drops bottle (not using a pin to perforate), hygiene, dosage and frequency to be followed, how long to wait between two medications, how and when to dispose of a medicine, and any special storage instructions (refrigeration, etc.).

Enhancing adherence to medication

Counselling during dispensing is important and should include information about why and how to take the medication. Where necessary, explain about drug-drug or food-drug interactions. The information should be provided in simple and clear language that the patient can understand. These oral instructions should be accompanied by printed or digital information for future reference. A QR code printed on the prescription can help patients and their family to access this information at a later date (see Figure 1).

Figure 1 After getting their medicines, patients at Aravind Eye Hospital take the prescription home. The prescription shows the name of the eye drops, which eye(s) to use them for, how many days to use them, how often, and how many drops to use. The QR code (top right) links to a video that explains how to instil the drops.



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How to Apply Eye Drops?
கண் சொட்டு மருந்துகளை பயன்படுத்துவது எப்படி?

DRUG PRESCRIPTION

[redacted]. 64 yrs / Male

Date: 13/03/2023
UIN [redacted]
MRN [redacted]

Medication மருந்து	Eye கண் Right வலது	Eye கண் Left இடது	Days நாட்கள்	Frequency / வேளைகள் Timing நேரம்	Frequency / வேளைகள் Count அளவு
1 AQUALUBE 10ML EYE DROPS	✓	✓	30 (13/03/2023 to 11/04/2023)	2 Times a day	1 drop

Review: After 1 year, on 13 Mar 2024
(மறுபரிசோதனை)

Dr. Sanjana 8.02.AM
UNIT-1 Reg No:132187

ANNAI MEDICALS
1, Anna Nagar, Madurai 625020, Ph:0452-4356105, Ext: 155 Fax No: 0452-2530984

Considerations when developing a standard drug list or formulary

An essential first step is to set up standard treatment protocols and a standard operating protocol for patient examination.

Include medicines based on evidence of efficacy. The World Health Organization's Model List of Essential Medicines is a good place to start (sections 14.1 Diagnostic agents: Ophthalmic medicines and 21. Ophthalmological preparations). The latest version is available from **https://bit.ly/WHO-em**.

Ensure that the list not only has the "best" medication, but also includes affordable alternatives that are locally available. Review the list by continuously monitoring outcomes and looking out for new alternatives.

The standardised drug list should be communicated to the following people working in the hospital: doctors, counsellors (nurses or allied health personnel who counsel patients), pharmacists, and the people responsible for inventory management and purchasing. Some government-run eye facilities receive medications from the government without the option to choose brands or vendors. In such cases, hospital managers should advise purchasing officers about which drugs to order.

Figure 2 Medicines are clearly labelled with numbers, which are repeated in the instructions (or prescription) sent home with patients.

To make it easier for patients who have to use multiple medications, we add coloured or numbered labels (Figure 2). The prescription also refers to this number. This makes it easy for everyone to follow instructions, not just for those who are unable to read.

For patients taking medications for chronic conditions, counselling should include the importance of long-term adherence and instructions on how and where to get refills.

Adverse drug reactions

Adverse drug reactions are undesirable events that follow the use of a drug. This can range from a simple rash to serious conditions, such as pulmonary oedema. Every drug reaction must be documented and analysed to understand whether the reaction is due to the medication itself, an interaction with another medicine, or whether there is an issue with a particular batch of medication.

Having a structured reporting system for this helps pharmacovigilance committees or local health care associations to track adverse drug reactions across the country, so they can make a collective decision on medicine about medicines and how to manage adverse reactions.

Reference

1 Kalita IR, Singh HV, Veena K, Mouttappa F. Primary eye care in pediatric population-I study (PREPP-I study): Demographic and clinical profile of pediatric patients treated in six major vision centers of a tertiary eye care facility in South India. Indian Journal of Ophthalmology.

Further reading

Two previous issues of the *Community Eye Health Journal* contain useful and relevant content related to managing medicines.

Comm Eye Health Vol. 34 No. 111, 2021. Running a safe eye service for patients and personnel **bit.ly/SafeEye**

Comm Eye Health Vol. 24 No. 76, 2011. Instruments and consumables. **bit.ly/CEHJ76**

How to use your eye medication

Once you have your medication, what is the procedure you should follow?

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Before you start

1 Assemble the items you need: the medication, clean tissue paper or paper towel, mirror, soap and water, or hand sanitiser (note: hand washing is preferred).
2 Read the written instructions on how to use each of the medications. This could be on the bottle, on the package insert, or on a separate sheet given to you at the hospital or pharmacy.
3 If using a drop, gel, and/or ointment, use them in this sequence; drop first, then gel, and then the ointment.
4 If the medicine is for treating a problem on your eyelid, it should be administered on the eyelid and not in the eye.
5 Do not instil medication into an eye that has been injured. Visit the eye clinic for review of the injury as soon as possible.
6 If the eye has discharge, clean the eye using sterile cotton wipes dipped in cooled, boiled water or bottled water before instilling the medication.

Preparation

1 Take off your spectacles if you are wearing any.
2 Wash your hands with soap and water and dry them using a paper towel. Hand washing is preferred, but if you are in a situation where this is not possible, you can use hand sanitiser instead.
3 If you are wearing contact lenses, take them out — unless your doctor has told you to leave them in.
4 Place a clean tissue or paper towel on the nearest surface.
5 If using eye drops, shake the bottle gently.
6 Remove the cap and place on the tissue or paper towel. Do not touch the tip. Make sure the dropper (or tube) and the cap stay clean.

If you are instilling the drops yourself:

1 Tilt your head back, open both eyes and look up towards the ceiling. Focus on a specific point on the ceiling. Do not blink or wipe the eye.
2 With the thumb and forefinger, pull your lower lid down and outwards to expose the lower conjunctival sac: the pocket where you instil the medication. You can stand in front of a mirror, or ask someone to hold a smaller mirror for you.
3 Hold the dropper bottle or tube between the thumb and index finger of your other hand. (If someone is helping you, they can hold the dropper bottle or tube and instil the drops or ointment.)
4 Position it so the tip is directly over the eyelid pocket.
5 Ensure the tip is not touching the eye, eyelids, or eyelashes; this avoids contaminating the drug.
6 Squeeze the bottle or tube gently to instil the eye drop (just one drop) or gel into the pocket (conjunctival sac), as instructed. Avoid letting the medication make contact with the sensitive cornea.

How to instil eye drops. INDIA

Getting the dosage correct

1 You may feel the cold drop or gel/ointment once it enters the eye, especially if the medication was stored in the refrigerator.
2 As long as you feel the medication in your eye or on the edge of the eyelid, you've been successful. You don't need to add more than one eye drop. The drop may spill over onto your cheek; this is okay as long as you felt it hit the surface of your eye.
3 If the medicine falls on your face or clothes or floor, but not actually into the eye, try again.
4 After instilling the drop, shut the eyelids lightly for a few seconds (up to one minute) while pressing your finger lightly on the inner corner of our eye, nearest your nose. This is known as the canthus and is the location of your tear ducts (visible as small holes). Doing this prevents the medicine draining into your nose, which improves absorption of the medicine where it is needed most – in your eye. Try not to blink.
5 If any liquid drops leaked out from your closed eyelids, blot around your eyes using a clean tissue or paper towel to remove the excess.
6 Repeat the steps with the other eye, if instructed to do so.
7 If using more than one type of eye drop, wait for 5–10 minutes between each of the different medications.
8 Wash hands with soap and water when done.

Improving adherence with eye medication: a patient-centred approach to prescribing

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Managing infectious eye conditions such as ulcers, or chronic conditions such as glaucoma, requires that patients regularly instil eye medication, often for long periods of time. How can prescribers support patients to do so?

Giving patients the right medicines starts during the prescribing process. INDIA

For eye medications to work, they must be used as prescribed and for as long as needed. In chronic diseases, such as glaucoma, this is for life.

There are many challenges when it comes to medication adherence. These include the availability and affordability of the medication, instilling the medication correctly, remembering when to do it, and doing it always, as is the case with long-term or chronic eye conditions.

Clinicians must therefore carefully consider patients' ability to adhere to a medication regimen when deciding how to manage their condition. For example:

- Should we admit the patient with a serious corneal infection, or send them home with eye drops?
- If a patient has glaucoma, should we prescribe eye drops to lower intraocular pressure (IOP), or offer surgery/laser?

What is adherence?

We prefer to use of the term 'adherence' instead of 'compliance' when talking about how well a patient is able to follow the medication regimen that was agreed between them and the prescriber/clinician.

The term 'compliance' is associated with the idea that a patient must follow a set of instructions imposed on them. When health care workers adopt this perspective, patients may be viewed as a passive recipient of health care, and health workers may blame or shame them if they don't use their medication as prescribed.

"The term 'adherence' recognises that a prescription is the result of a joint decision-making process between the patient and the clinician."

The term 'adherence', however, recognises that a prescription is the result of a joint decision-making process between the patient and the clinician. This recognises the patient as an active participant in their own health care (or a co-producer of health) and acknowledges their right to choose as well as their individual circumstances and challenges. When something goes wrong, and a patient does not adhere to the prescribed medication regimen, health workers who adopt this perspective can work with patients to explore causes and solutions.

Prescribing to support adherence

Consider the following aspects when deciding on the best medication regimen for your patients.

- The local **availability** of the medication, and patients' **ability to pay**. If it is not available locally or is too expensive, consider an alternative medication or other treatment options such as surgery, if appropriate. If it is not covered by health or medical insurance, or not on the list of medicines approved (or provided) by your country's health service, consider advocating for change. Generic medications are an important alternative where available as they are often cheaper and as effective as the expensive branded products.
- The **complexity** of the patient's overall medication regimen. Ask what other medication a patient is taking, particularly long-term medication, and consider any adverse drug interactions that could lead to the patient discontinuing their eye medication. You can also help patients to remember to use their eye medication, e.g., by suggesting that they instil eye drops at the same time of day as they would normally take their long term medication or time the instillation of medication with routine activities they carry out daily, such as prayer times for muslims.
- **Support networks.** Does the patient have family members or others who can remind them to take their medication, or motivate them to continue when they want to stop? It is always important to

counsel a trusted family member, partner or friend on the medications the patient is being given so they can help them maintain adherence by reminding them and helping them to instil the medication.

- Patients' **physical health**. This can include their ability to administer eye medication, for example, if they suffer from arthritis. Can someone else help them? Find out if there are installation aids available locally, which make it easier for patients with conditions such as arthritis to instil their own drops.
- Patients' **cognitive health**. Patients with cognitive impairments, dementia, or attention deficit disorder may struggle to remember when to use their eye drops and may require support from others or electronic reminders (e.g., by programming mobile phones to remind them of medication times).

A note on patient comfort

Stinging sensation or blurring of vision is a common side effect of many eye drops. As this is transient, it is usually better to educate the patient about this possibility and teach them to cope if it is not severe, as changing medication may not be possible, or will be prohibitively expensive. One exception is chlorhexidine, which can be locally manufactured using a buffer solution which reduces stinging sensation.

ADVOCACY

Inclusion of eye medication in national health care systems

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Advocacy for eye medicines is easier with these helpful resources and guidance.

With so many eye medicines available, the WHO model list provides helpful guidance. INDIA

The World Health Organization (WHO) maintains a model list of essential medicines. The essential medicines include those that satisfy the priority health care needs of a population. The medicines are the most effective, safe, evidence-based available and are comparatively cost-effective. They are intended to be available in health systems at all times. WHO recommends that countries make these medicines available in the appropriate form and dosage, and ensure that they are available, accessible, and affordable to everyone in need. Universal access can only become possible only when medicines are included in a country's essential medicines list and funded by the national health financing system.

The WHO model list of essential medicines includes ophthalmic medicines in section: 14.1 diagnostic agents: ophthalmic medicines; and section 2: ophthalmological preparations. This information needs to be communicated to the policy makers and referred when advocating for universal eye health. The latest list is available here:
bit.ly/WHO-em

The WHO's Package of Eye Care Interventions (PECI), launched at the World Health Assembly in 2022, is a set of evidence-based eye care interventions and the resources needed for their implementation. PECI – which includes the list of ophthalmic medicines in the WHO essential medicines list – is designed to support policy makers and technical decision makers to integrate eye care into the health care services system of a country. This tool is an important resource when advocating for the inclusion of essential eye medicines in a national essential medicines list and in health financing benefit packages.

When advocating for eye medicines, also refer to the United Nations' Sustainable Development Goals, target 3.8. This target focuses on achieving universal health coverage, including financial risk protection, access to high quality essential health care services and access to safe, effective, high quality affordable essential medicines and vaccines for all. Without provision for equitable access to essential medicines for eye conditions, achieving universal eye health coverage is not possible.

Access to essential ophthalmic medicines also aligns with the principle of integrated people-centred eye care (IPEC). The IPEC was adopted by the 73rd World Health Assembly resolution in 2020. To know more about advocating for IPEC, check out IAPB's IPEC Advocacy to Action Toolkit. The toolkit includes PowerPoint slides, letter and IPEC policy brief templates that can be adapted and used to approach stakeholders for policy dialogues.

The WHO has also produced guidelines on using the WHO Model List of Essential Medicines to update the national essential medicines list. See **https://bit.ly/useWHOem**

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Valuing pharmacists as members of the eye team

Pharmacists have extensive knowledge about the ever-increasing number of eye medicines available; their input is vital to protect patients and ensure effective treatment.

Pharmacists are valuable members of the eye team. They can support the eye care team to make effective, patient-centred decisions by sharing their extensive knowledge about:

- the range of medicines available locally for eye conditions
- the interactions between different medicines
- how to improve adherence, e.g., by suggesting a change in the type of bottle being used, or a change in formulation (e.g., with a preservative-free product to reduce stinging sensation).

The role of the hospital pharmacist as part of a multidisciplinary team is usually understood and accepted. However, the role of the community pharmacist may not be well understood.

In the community setting, the pharmacy is often seen as a simply the location at which patients collect their medication. The community pharmacy is, however, an essential point of contact for primary health care, including primary eye care. Patients come to seek advice about a wide range of conditions and about over-the-counter or prescribed medication.

Community pharmacists play an essential clinical role in assessing the nature of patients' primary concerns (e.g., is it allergic, infective, or acute?) and deciding whether they need to be referred. Pharmacists can also offer support, information, and reassurance to their patients.

Good working relationships

Effective teamwork between community pharmacists and other members of the eye team is essential to ensure patient safety and improve patient outcomes, so it is therefore important to create opportunities for collaboration and to set up effective communication channels between community pharmacists and the eye team. Here are a few ideas.

Prescription checking

- Recognise that prescription errors are often picked up by pharmacists, who are specifically trained to do so. Acknowledge that this is in the best interests of both patients and doctors. Acknowledge that this is in the best interests of patients and doctors. Respect pharmacists' role and training.
- Share the eye team's contact details with community pharmacists, so that it is easy and convenient for pharmacists to resolve queries and potential errors.
- When giving patients a prescription to take to the pharmacy, it may be helpful to attach a copy of their hospital or discharge notes (containing their diagnosis, the medication they have been prescribed, and the dates of any follow-up appointments). This will make it easier for the pharmacist to detect inconsistencies or prescription errors. (In the UK, patients who leave the hospital receive a 'discharge summary' which is shared with pharmacists via an electronic medical records system; this allows pharmacists to follow up on the prescribing and dispensing of medication for each patient.)

Referral and feedback

Set up a referral and feedback mechanism between the eye clinic and community pharmacists.

- Ensure pharmacists have up-to-date information about clinic days and times, so patients don't have the expense of a wasted journey.
- Give feedback to pharmacists who refer patients to you. For example, you can thank them for referring the patient, confirm whether or not they were right to refer them, and offer support or guidance to improve future referrals.
- You could be proactive and give all the community pharmacists in the area a set of referral forms with your hospital or clinic details and space for them to add their contact details, the reason for referral, and to indicate whether or not this is an emergency.
- The clinic administrators can also send the patient's discharge information directly to the pharmacist.

Training

The multidisciplinary eye team does not stop at the hospital door – it extends out to the community. Some ideas for bringing community pharmacists into closer contact with the hospital-based eye team include the following.

- Offer training sessions for community pharmacists and outreach nurses/eye care workers. Offer sessions on basic eye care, specialist sessions, e.g., eye infections or glaucoma care, or practical sessions such as referral guidelines and procedures
- Invite pharmacists to share their knowledge about the latest eye medications or formulations. This is a great opportunity for learning for all members of the multidisciplinary eye team to learn about the role of community pharmacists/nurses.

Care for long term eye conditions

- For chronic eye conditions such as glaucoma, the community pharmacist may see the patient more often than the ophthalmologist. Sharing the patient's care plan with the pharmacist can help, as every contact they have with the patient is an opportunity for them to support adherence and safety, and to reinforce key messages.

Pharmacy in eye care is an ever-growing industry, with new drugs and formulations coming onto the market every few months. Pharmacists undergo many years of training, and their input is vital to ensure patient safety and effective treatment. They can advise clinicians about potential interactions, suitability, availability, and alternatives. Therefore, collaborating closely with community pharmacists will help eye care providers to offer effective and safe treatment options in both hospital and community settings.

Further reading

Waszyk-Nowaczyk M, Guzenda W, Kamasa K, Pawlak K, Bałtruszewicz N, Artyszuk K, Białoszewski A, Merks P. Cooperation between pharmacists and physicians – Whether it was before and is it still ongoing during the pandemic? J Multidiscip Healthc. 2021 Aug 7;14:2101-10. **https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8357703/**

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The impact of oral and systemic medications on the eye

Knowing which systemic and oral medications can affect eye health, and how their adverse effects present, can help you to identify and manage patients correctly.

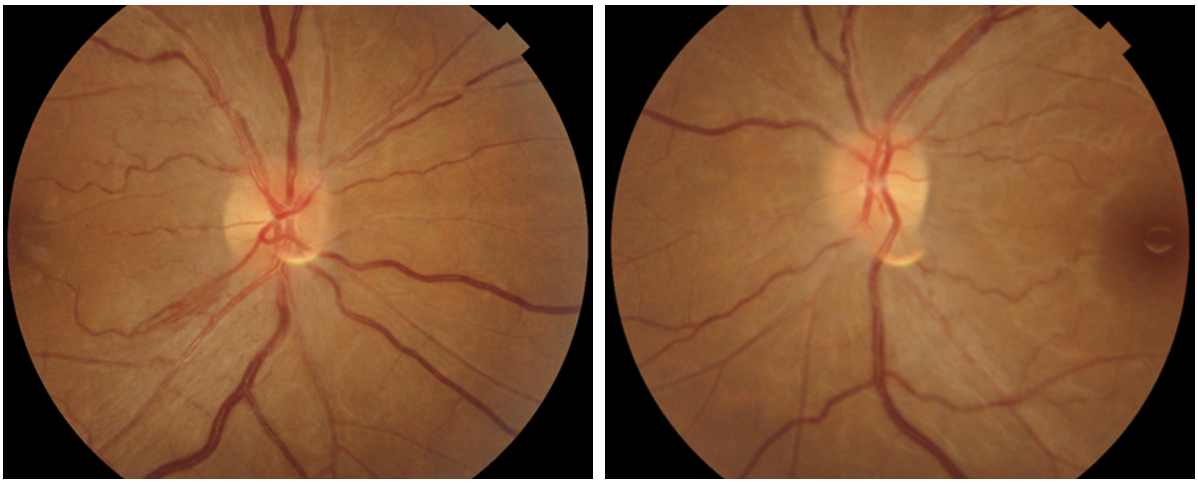


Figure 1 Bilateral toxic optic neuropathy with disc oedema in a 32-year-old female patient with a history of ethambutol intake and on tacrolimus after a renal transplant

A variety of oral and systemic medicines can have a harmful effect on the eyes.[1] Some of the adverse effects may be dose-related, while others may not be.

Patients may not be aware of the relationship between the medication and their eye condition, and may not think to mention this to you, unless you specifically ask what medicines they are currently taking. They may not remember the name of their condition or the names of the medicine.

It is therefore helpful to be familiar with the different adverse effects of oral or systemic medications, so you can better identify and manage the eye condition the patient presents with. In addition to reporting the adverse reaction via the usual channels, it is advisable to contact the clinician who prescribed the medication so they can consider alternatives.

Reporting of adverse drug reactions

There are national adverse drug reporting centres in 153 countries worldwide. Reporting of adverse reactions is mostly voluntary, and is done by health care professionals. At the global level, the World Health Organization Programme for International Drug Monitoring collates the reports from the national centres to ensure timely identification of suspected safety problems. To find out more, including how to set up an adverse drug reporting centre in your country, visit **https://bit.ly/DrugWHO**.

In addition to eye care professionals, physicians prescribing these drugs must also be made aware of any potential adverse reactions. That would enable them to warn the patients to report early symptoms and to undergo regular eye check-ups wherever indicated. A list of medications which can cause ocular toxicity is given in Table 1.

Remember:

- Patients are unlikely to tell you what other medication they are taking, unless you ask.
- Some patients may not remember the name or dosage details, so you may need to check their records, if available.

Some adverse reactions can affect vision and are potentially sight-threatening, while others may not cause loss of vision but can lead to hazy vision or discomfort.

Sight-threatening adverse reactions

Raised intraocular pressure

Patients may present with raised pressures in the eye caused by the intake of the following drugs.

- **Corticosteroids** (such as prednisolone or dexamethasone)[2] are used as long-term medications for some joint disorders, skin diseases, auto-immune disorders and in transplant patients. They are administered by various routes: topically, orally, intravenous, nasally or as injections in joints and can raise intraocular pressure, resulting in secondary glaucoma.
- **Antihistamines, beta blockers, antidepressants, antipsychotics and some diuretics** can cause angle-closure glaucoma in pre-disposed patients who have shallow anterior chambers. These are drugs with anti-cholinergic effects and are used to treat conditions like urinary incontinence, chronic obstructive pulmonary disorder, allergies, or mental health conditions. This group of medications generally causes pupillary dilation leading to angle closure. Some sulfa-based drugs are also known to cause a similar reaction.[3]
- **Topiramate**, which is used to treat epilepsy, can cause uveal effusion with very high intraocular

pressure. The symptoms include blurred vision, difficulty seeing, and eye pain, and usually happen in the first month of taking the medication.

Patients on these drugs must be monitored for intraocular pressure (IOP) and AC depth. Some patients are 'high responders' and can have significantly increased IOP. In case, corticosteroids cannot be tapered or replaced, IOP must be controlled medically.

Cataract

- **Corticosteroids.** Long-term use of corticosteroids can also lead to posterior sub-capsular cataract. This form of cataract leads to vision-related issues early in its course and may warrant early surgery.
- Some other less-used drugs known to cause cataracts include **phenothiazines**, used for behavioural disorders and **busulfan**, an antineoplastic drug.[3]

Toxic optic neuropathy

Patients with toxic optic neuropathy may present with bilateral, painless loss of vision (Figure 1). This has been reported with various drugs[4]:

- **Ethambutol** and **isoniazid**, which are commonly prescribed for tuberculosis in countries where tuberculosis is endemic; the risk of toxic optic neuropathy is greater in patients who also have renal disease
- **Ciprofloxacin** and **chloramphenicol**, both antimicrobial medications
- **Antimetabolite medicines** used in the treatment of malignancies
- **Amiodarone** used for arrhythmias
- **Amoebicidal medications**.

Patients on these drugs must be screened for visual acuity, colour vision, and central vision testing. The majority of these defects can be reversed with timely discontinuation and thus, timely monitoring is essential.

Retinal haemorrhages and internal ocular bleeding

Bleeding in retinal tissues can lead to sight loss. This may be caused by the following medication:

- **Anticoagulants**[5] used for the prevention of heart disease and stroke
- **Antineoplastic drugs** used for malignancies.

This can be monitored using blood tests and medication may need to be discontinued in some cases, especially where a minor bleed has already occurred. These drugs can also lead to bleeding during eye surgery and may have to be discontinued prior to some eye surgeries. It is therefore vital that eye surgeons know about patients' usage of such drugs.

Retinal toxicity

Some drugs can cause damage to one of the layers of the retina (retinal pigment epithelial loss). Unfortunately, some of these patients may already have central visual loss when they present. Retinal toxicity is irreversible, thus early recognition by regular screening, and early discontinuation, is imperative.

- **Chloroquine** and **hydroxychloroquine**[6] are antimalarial drugs. They are more likely to cause retinal toxicity when used for longer periods of time, either to treat other inflammatory conditions of the joints or – more recently – as prophylaxes for COVID-19.
- **Thioridazine** and **chlorpromazine** are phenothiazines used for the treatment of anxiety, depression, and other behavioural disorders.

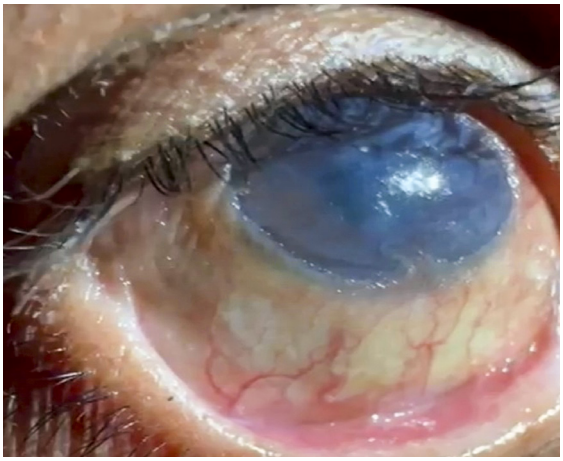
Check patients' vision using manual or automated visual field testing or spectral-domain optical coherence tomography (if available). Multifocal electroretinogram (mfERG), if available, can be used for objective corroboration with visual fields.

Other potentially sight-threatening adverse reactions to medication

- **Central serous retinopathy.** Corticosteroids can cause central serous retinopathy (CSR) in some patients.
- **Intracranial hypertension.** Tetracycline, which is used long-term for conditions like rosacea can lead to intracranial hypertension or pseudotumor cerebri, which may lead to optic atrophy if left untreated.
- **Stevens-Johnson syndrome.** This is a relatively rare drug reaction, characterised by skin and mucosal involvement. It has an acute phase with severe pseudomembranous conjunctivitis (Figure 2) and a chronic phase with extreme dry eye and cicatricial features (Figure 3) and can be caused by common drugs such as painkillers or cold and flu medication. Over one hundred drugs have been associated with this syndrome.[7] In the acute phase, treatment includes management of pain, topical and systemic anti-inflammatory medications, and antibiotics to control infection.

Figure 2 A 12-year-old child with acute Stevens-Johnson Syndrome. **INDIA**

Figure 3 A 27-year-old man with sequelae of Stevens-Johnson Syndrome. **INDIA**



Non-sight-threatening adverse reactions

These side effects may cause discomfort but may not be directly sight threatening.

Corneal vortex keratopathy

This is a whorl-like pattern on the cornea and is generally not visually significant. These are mostly caused by amiodarone, a drug used to treat cardiac arrhythmia. Some of the other drugs which can cause this are chloroquine, hydroxychloroquine, indomethacin, and tamoxifen.[6] The dosages need to be reduced only if the corneal condition causes extreme discomfort or blurring of vision.

Floppy iris syndrome

Another specific drug-induced condition is one in which there is an effect on the constrictor muscles of the iris, leading to poor dilation and floppy iris during cataract surgery. This is generally caused by alpha-1 blockers like tamsulosin (used for prostatic hypertrophy).[8] These technical issues during cataract surgery can be prevented if adequate precautions are taken, so patient's usage of these drugs must be known to the surgeon. It is sometimes recommended that tamsulosin be stopped two weeks before surgery, but it may be more important that the surgeon is made aware that the patient is taking one of these drugs.

Dry eye

A diverse group of orally administered medications have been linked with dry eye. These include antihypertensive drugs such as atenolol and acebutolol, antihistamines such as cetirizine, antivirals such as aciclovir, analgesics (e.g., ibuprofen) and some antidepressants, antipsychotic, and anti-arrhythmic medications (see Table 1).[3] Other conditions, like epiphora, blepharitis, and conjunctivitis can also be side effects of some anti-malignancy drugs that are administered systematically.[9]

Table 1 Drugs that can cause ocular toxicity.[1]

Oral drugs	Use	Possible ocular side effects
Topiramate	Treatment of epilepsy	Secondary angle-closure glaucoma, visual field defects, oculogyric crisis, uveitis
Gabapentin	Treatment of epilepsy	Nystagmus, diplopia and visual field defects
Vigabatrin	Treatment of epilepsy	Visual field constriction, optic nerve atrophy
Bisphosphonates (e.g., alendronate sodium,, risedronate, zoledronic acid	Treatment and prevetion of osteoporosis	Inflammation in the eye leads to conjunctivitis, episcleritis, scleritis, keratitis or uveitis, or corneal and scleral melting
Chloroquine-based drugs (chloroquine, hydroxychloroquine	Treatment of malaria	Maculopathy, peripheral retinopathy
Corticosteroids (e.g., prednisolone, dexamethasone)	Anti-inflammatory	Corticosteroid-induced raised intraocular pressure can lead to glaucoma, acceleration of cataract progression, and subcapsular cataracts.
Ethambutol	Treatment of tuberculosis	Optic neuropathy characterised by bilateral central visual loss, decreased colour vision, central visual field defects, and (eventually) optic atrophy
Fingolimod	Treatment of multiple sclerosis	Macular oedema, blurred vision, distortion, and impaired reading vision
Isotretinoin and vitamin A	Acne and vitamin A deficiency treatment, respectively	Blepharoconjunctivitis, chalazia, corneal opacities, dry eyes, retinopathy
Mitogen-activated protein kinase kinase enzyme (MEK) inhibitors, e.g., crizotinib	Treatment of advanced non-small cell lung cancer	Decreased visual acuity, visual field defects, dry eye symptoms, eyelid abnormalities, retinal vein occlusion, and retinopathy
Pentosan polysulfate	Relief of bladder pain and discomfort related to interstitial cystitis	Maculopathy, retinal pigment epithelial lesions
Phenothiazines	Treatment of schizophrenia and other psychotic disorders	Abnormal pigmentation of the eyelids, conjunctiva and cornea. Corneal epithelial changes (high dose). Corneal oedema (rare).
Phosphodiesterase type 5 inhibitors, e.g., sildenafil, tadalafil	Treatment of erectile dysfunction	Persistent blurred vision, non-arteritic ischaemic optic neuropathy, cilioretinal artery occlusion, or central serous chorioretinopathy.
Tamoxifen	Treatment of breast cancer	Intraretinal crystalline deposits, macular oedema, and punctate retinal pigmentary changes.
Tetracyclines, e.g., doxycycline, tetracycline	Antibiotics	Nausea, vomiting, and morning headaches may be symptoms of idiopathic intracranial hypertension which can lead to permanent loss of vision
Thiazolidinediones, e.g., glitazones, pioglitazone, rosiglitazone	Management of type 2 diabetes mellitus	Macular oedema

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Local production of eye drops in the hospital or pharmacy setting: considerations and safety tips

Some eye drops can be locally prepared to improve patients' access to medication. Here is what you will need to consider.

Eye drops preparation in Ruharo Mission Hospital. UGANDA

Most eye medicines for topical use are prepared by pharmaceutical companies using special automated mixing and filling machines. However, some eye drops can be prepared in a pharmacy setting in a hospital. There are several reasons[1,2]:

- Patients may be unable to afford commercially available eye drops, and locally prepared eye drops are often more affordable.
- Eye drops may be unavailable due to manufacturing shortages or because a product is discontinued; this can be overcome by preparing eye drops in hospital or pharmacy settings.
- Combinations of drugs that are not commercially available might be prepared locally; for example, eye drops combining anaesthetic and dilating agents.
- In some cases, the drug might be available in a formulation or strength that is not intended for ophthalmic use and needs to be adapted. One example is the preparation of amphotericin B eye drops from intravenous solution.
- Some eye drops need to be patient specific and therefore prepared individually; for example, autologous serum eye drops that are compounded using the patient's own serum.

The main ingredients for preparation of topical ophthalmic eye drops usually include:

- The active pharmaceutical ingredient (API), either as powder or as a concentrated solution.
- A solvent: either sterile water or buffer solution
- A preservative: an antimicrobial agent added to the eye drops to prevent microbial contamination of the liquid during use.

In general, eye drops are prepared in one of two ways:

1 Dissolving the active pharmaceutical ingredient/ preservative (in powder form) in a suitable vehicle (either sterile water or a buffer solution).

2 Diluting a concentrated solution of the active pharmaceutical ingredient using sterile water or buffer solution.

There are several important elements that should be considered when preparing eye drops.

1. Sterilisation

Eye drops must be sterilised to ensure they are free of microbial contamination. The method of sterilisation depends on the stability of the drug at high temperature.

The options are:

- **Autoclaving.** Autoclaving is used to sterilise pharmaceutical products (solutions, suspensions, powder) which are stable at high temperature[1]. Eye drops in the final packaging (filled and sealed eye drop bottles) are usually sterilised at the end of the production process (terminal sterilisation) using autoclaving (saturated steam at 121–132°C) for 15 minutes to kill microorganisms.[1]
- **Filter sterilisation.** If the drug is not stable at high temperatures, eye drops in solution form can be sterilised by filtration through a 0.22 µm filter into a sterile final container. This method is called filter sterilisation and it should be conducted under aseptic conditions using a laminar flow cabinet. Filter sterilisation is not suitable for use with eye drops in suspension form, as the 0.22 µm filter will remove the finely dispersed drug particles and make the eye drops ineffective.

2. Inherent toxicity of the drug

The pharmacist should check the drug-specific data safety document (the drug safety data sheet) to get information about the toxicity of the drug. The

pharmacist should adhere to the established guidelines for handling each drug.[3]

3. Removal of particulates

All compounded eye drop solutions should be filtered using a 5 µm filter to remove any visible particulate matter.[2] This can be done using glass sintered filters or polypropylene fibre filters under minimal pressure. This pressure can be generated using either a hand-held or foot suction pump.

4. pH

The pH of eye drops is important for drug solubility and for the stability of some drugs.[3] For optimal ocular comfort, it should be similar to the pH of natural tears (pH 7.4). However, sometimes it is not feasible to prepare eye drops with pH 7.4 due to drug stability or solubility issues. The acceptable pH range for eye drops is in the range of 6.5–7.8 to ensure patient comfort. A more acidic or alkaline pH can induce tearing, discomfort and pain.[4,5] A suitable buffer can be used to control and maintain the pH of the eye drops during storage, such as citrate or acetate buffer.

5. Tonicity

Tonicity is defined as the ability of water to enter or exit through a membrane (e.g. cell membrane), via osmosis. The tonicity of the eye drops depends on the concentration of dissolved solutes (e.g. buffer salts and the active pharmaceurical ingredient). Ideally, the tonicity of eye drops should be similar to natural tears, which have a tonicity equal to 0.9% saline. In general, a range of 0.5–2% saline tonicity is well tolerated by most patients. Hypertonic solution (higher than the tonicity of 0.9% saline) can cause tearing. This increase in tear flow reduces the concentration of the drug in the eye, leading to reduction of drug efficacy.[3,6] Hypotonic solutions (lower than tonicity of 0.9% saline) do not cause tearing, but might cause ocular discomfort.[3,6]

6. Preservatives

The addition of preservatives to multi-dose eye drops is crucial to prevent secondary contamination during storage and application.[7] Several studies have reported severe ocular infections related to preservative-free ophthalmic preparations prepared in local pharmacy settings.[7,8]

Selection of suitable and safe preservatives is important.[7] Eye drops that are intended for long-term use, e.g. for chronic eye conditions, should ideally be preservative free. These medications are not suitable for local production as they require highly specialised production facilities and special packaging, e.g., single-use packaging that avoids contamination during use. **Note:** some drugs, such as chlorhexidine, do not require the addition of preservative when prepared in the form of eye drops, because the drug itself acts as a preservative.

7. Stability

The drug should be stable in the selected solvent (e.g., buffer solution or sterile water). The stability of eye drops prepared within hospitals or pharmacies should be assessed according to the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) guidelines to determine the optimum storage conditions and drug shelf life.[9] The shelf life (expiration date) should be determined based on the documented stability data and the potential for microbial contamination.[2] The chemical stability of the active pharmaceutical ingredient(s), preservatives, other excipients (non-active pharmaceutical ingredients), and packaging should be considered when assessing the overall stability of the final ophthalmic product.[2]

8. Packaging and storage of the final product

The final container/packaging should be suitable for ophthalmic use and should not compromise the stability and efficacy of the topical preparation.[2]

Many compounded ophthalmic eye drops can be packaged in either sterile plastic bottles with integrated dropper tips (a standard eye drop container) or in glass bottles with separate droppers. The stability of some eye drops might be affected by the type of eye drops container used; for example, cyclosporine is absorbed by polyvinyl chloride, a polymer used in some plastic dropper bottles.

Safety tips

According to the American Society of Health-System Pharmacists (ASHP) Pharmacy-Prepared Ophthalmic Products guidelines, the following should be considered when preparing eye drops in the pharmacy/hospital setting[2]:

- Adhere to aseptic techniques and sterilisation procedures to ensure that eye drops are sterile (free from microbial contamination).
- Ask a colleague to double check your calculations of the amount of each ingredient that will be used in preparing the eye drops; this will minimise error.
- All ingredients should be mixed in sterile, empty containers. When using more than one container for compounding a sterile preparation, each container should be labelled.
- Compounding should be performed in a certified laminar airflow hood or, for a cytotoxic or hazardous product, inside a biological safety cabinet.
- The compounded eye drops should be clearly labelled according to the hospital or pharmacy policy for prescription labelling. The label should contain information about the concentrations of active ingredients and preservatives and information about storage conditions, handling requirements, and expiration dates.
- The storage instructions on the label should be clear. For example, room temperature means 15–25 °C, refrigerator means 2–8 °C, and freezer means below 0°C.

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How to prepare chlorhexidine eye drops

Preparing chlorhexidine eye drops in a buffered acetate solution can help to improve patient comfort; here is how.

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Figure 1 a. pH meter to measure the pH of buffer solutions and eye drops. **b.** Conductivity meter for water analysis.

Chlorhexidine eye drops can be used for the treatment of fungal keratitis as a second line therapy where natamycin eye drops are not available.[1,2] Chlorhexidine eye drops typically used in the clinic are prepared by diluting a concentrated solution of chlorhexidine using sterile water without controlling for pH or tonicity[3] and are reported to cause patient discomfort (stinging sensation). The pH and tonicity of chlorhexidine eye drops can be controlled by using acetate buffer (141.4 mM, pH 6.75) to improve patient tolerance/comfort.[3] Controlling the pH of the chlorhexidine eye drops can also improve the stability of the drops: chlorhexidine eye drops prepared using acetate buffer (141.4 mM, pH 6.75) were shown to have stable pH (~6.75) and drug concentration at 40 degrees Celsius for 21 months.[3]

In this article, we share the protocol we used for the local preparation of acetate-buffered chlorhexidine eye drops at Ruharo Mission Hospital's eye drop production facility in Uganda.[3] This protocol will produce 2,000 ml of buffered chlorhexidine eye drops, which is enough to fill 200 bottles containing 10 ml eye drop solution per bottle.

Facilities/space

Ideally, eye drops should be prepared in a certified clean room equipped with an air control system complete with a filter that removes dust and other potential sources of contamination. A laminar flow cabinet can be used for local preparation of eye drops in the certified clean room or in a normal room with air conditioning. In the absence of a clean room/air control system and laminar flow cabinet, we recommend you take the following measures:

- Use a room that is dedicated for eye drop production only, with air conditioning and a double door entry system to avoid air disturbance, minimising contamination (airlock system).
- Less than 2 hours before each eye drop production session, clean the floors and surfaces of the production room (or the room and airlock) by wiping with distilled water and an antiseptic (such as Dettol or cetrimide 0.5% w/v), followed by spraying with 75% ethanol. Follow the same cleaning procedure after using the production room.
- Once surfaces are dry, spray production surfaces with 70% ethanol to further reduce the presence of microbes.

What you will need

Ingredients

- Chlorhexidine digluconate solution (20% w/v)
- Sodium acetate
- Acetic acid (20% v/v)
- Sodium hydroxide (10 M)
- Freshly distilled water

Equipment

- Volumetric flasks (20 ml, 2000 ml) + stopper
- Measuring cylinders (10 ml and 1000 ml).
- Pipette (1 ml) and pipette tips
- Metal jug
- Filtration system (filter funnel, 5 µm filter membrane, filter clamp/support, vacuum pump, conical flask/bottle)
- Syringes (with 10 ml graduations)
- Amber glass eye drop 10 ml bottles
- Bottle lids – with or without dropper (Use HDPE or PP)
- Class II or electronic balance
- pH meter (Figure 1a)
- Conductivity meter (Figure 1b)
- Autoclave or steam bath
- Labels

Method

- Wash hands before entering airlock room.
- Wear protective clothes (production gown, gloves, boots, hair net or head cap, mask and eye protection) in the airlock room.
- Ensure the production room and equipment are clean.
- Rinse all containers three times using distilled water, by filling them to the top and then discarding the water. Then sterilise using an autoclave or water bath.
- Wash and sterilise the empty eye drop bottles at 121°C for 15 minutes.
- Wash the filtration system by filling it with hot distilled water, flushing it using a vacuum pump, and discarding the water. Repeat this three times. Then backwash the filtering system three times by reversing the filtering head and filling the filtration system with hot distilled water using a vacuum pump.
- Collect 2,500 ml freshly distilled water.

Prepare acetate buffer

- Dissolve sodium acetate (23.198 g) in 2,000 ml of freshly distilled water in a large mixing beaker. Then add 4.46 ml of acetic acid (20% v/v) to the sodium acetate solution and mix the solution.
- Using a portable pH meter, adjust the pH by dropwise addition of sodium hydroxide (10 M), adding approximately 1.938 ml to reach pH 6.75.

Prepare chlorhexidine 0.2% (2,000 ml batches)

- Measure 20 ml of 20% chlorhexidine using 20 ml volumetric flask.
- Transfer 20 ml of chlorhexidine (20%) into 2,000 ml volumetric flask (Figure 2). Rinse the 20 ml flask three times with buffer and transfer the rinsed solution into the 2,000 ml volumetric flask (Figure 2).
- Fill the 2,000 ml volumetric flask containing the chlorhexidine solution to 2,000 ml mark with the acetate buffer.
- Place lid on flask, invert flask and shake to stir.
- Assemble filter membrane onto filter bed and secure with clamp/support. Pass solution through filter into rinsed conical flask/ bottle using pump vacuum.
- Transfer filtrate into a jug or a bottle.

Figure 2 Volumetric flask (2,000 ml) for dilution of chlorhexidine 20% w/v to 0.2% w/v by addition of acetate buffer.

Dispensing

- Lay out the empty eye drop bottles on a clean surface.
- Dispense the eye drop solution using syringes or measuring cylinder or pressmatic pump dispenser in 10 ml portions into the amber glass eye drop bottles.
- Seal the bottles with tightly fitted lids (either polypropylene plastic dropper or HDPE cap) (Figure 3a) using a manual capping machine (Figure 3b) or by hand if a capping machine is not available.

Sterilisation

- Sterilise the bottles using a water steam bath at 100°C (at atmospheric pressure) for 30 minutes. If an autoclave is available, sterilise by autoclaving at 121°C for 15 minutes.

Visual inspection and quality control testing

- Do a visual inspection in bright light. Shake the eye drop bottle and observe the contents against white and black backgrounds to check for visible particles or debris (Figure 3C).
- Check lids cannot be tightened further.
- Check correct fill volume.
- Check for the presence of leaks by turning the filled eye drop bottles upside down.
- Send the first, middle, and last bottles of each batch for sterility testing and recall the batch immediately if any samples are positive for microorganisms.
- Check drug concentration, ideally using high performance liquid chromatography (HPLC). In case HPLC is not available, use a UV spectrophotometer to check the concentration of chlorhexidine in the eye drop solution.

Labelling

Allow the sterilised bottles to stand for at least 12 hours to cool and dry before labelling.

The label should contain:

- Name and strength of the drug: chlorhexidine digluconate 0.2% w/v.
- Composition of the eye drops: pH buffered in acetate buffer, no added preservative.
- Storage conditions: store below or at 25°C and protect from light. Once opened, store at 4°C and use within 7 days.
- Shelf life of unopened sterile bottles: 24 months at 25°C.

Figure 3 a. Amber glass bottles with PPE plastic droppers. **b.** Manual capping/sealing of bottles. **c.** Visual inspection area.

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Key community eye health messages

Before the patient leaves the clinic, ensure that they

- Have the correct number and type of medicines.
- Know how to safely manage their medication, including storing it properly, checking expiry dates, understanding the duration of treatment, and avoiding contamination of the medicines.
- Know how to administer their medicines correctly.

Common mistakes to avoid while instilling eye drops

- Retracting the upper lid instead of the lower lid. This can result in eye drops spilling over the eyeball, and the amount of medication that reaches the eye will be insufficient, leading to inadequate dosage for the patient.
- Retracting the lower lid but instilling more than one drop at a time. Patients may do this if they are not sure whether the first drop has gone in.
- Not allowing enough time between two different eye medications. The second eye drop formulation may "wash away" the first one out of the eye before it is fully absorbed. Consecutively, we may not see improvement, even after instilling medicine.

To avoid eye infections

- Always wash your hands thoroughly with soap and warm water before touching your eyes or instilling eye drops.
- Do not touch the tip of the dropper bottle.
- If the dropper bottle lid or ointment cap falls on the ground, pick it up immediately and clean it using a sterile alcohol swab before putting the lid back on.
- When working with chemicals, dust, or other potential irritants, wear protective goggles or glasses to prevent foreign objects or substances from entering your eyes.